the other being closed by a finger, and the mouth shut. Several deep inspirations should then be taken, as in snuffing heartily from a smelling-bottle.

CASE IV.—*Case of Dislocation of the Metacarpal bone of the Thumb.*—M. B., a tailor, accidentally fell down stairs, and in attempting to save himself, the weight of his body came (as he thinks) upon the extended thumb of his right hand. Considerable pain and swelling ensued, and the mobility of the thumb, though not lost, was much restrained. He presented himself two days after the accident. There was a projection under the skin, which could be easily pushed into its place, but immediately returned. It gave at first the idea of a dislocation of the trapezium, and had actually been taken for it by an intelligent friend, but its true nature was sufficiently apparent. In the course of five or six days, as many different kinds of splints and bandages were resorted to, to no purpose. A very small amount of force applied directly to the head of the bone sufficed to keep it in its place, but when sought to be effected through the aid of bandages and splints, unless applied so tight that he could not bear them, the head slipped out, the capsular ligament being torn. I had a clamp made of a piece of steel, a half an inch wide and one eighth thick and six inches long, bent into the shape of the letter U, with a screw passing through one end, perpendicularly to the surface. A compress was placed over the head of the bone, and one on the palmar aspect of the articulation, and a very moderate pressure from the instrument kept the bone in its place, and effected a perfect cure.

ART. XI.—*On the Action of Poisons.* By JAMES BLAKE, M. D., F. R. C. S. E., Professor of Anatomy at the St Louis University.

THE subject of the action of poisons, has attracted the attention of physiologists since this branch of science first began to be cultivated; and undoubtedly the remarkable effects which many of the more venomous substances produce on the living organism, are well calculated to excite the attention, both of the philosophical inquirer and of the lover of the marvellous. It is not, however, until within the last few years, that any well-devised experiments have been performed with this class of substances, so as to make them available in illustrating some of the phenomena of living beings. The researches of Fontana, Brodie, Orfila, Magendie, and Christison, have undoubtedly furnished us with many interesting facts on the action of poisons; and if, after all the labour that has been bestowed on it by these able experimenters, some of the more simple and fundamental problems connected with it have not yet received their solution, this dearth of useful results is not due so much to a want of care or accuracy, on the part of those who have instituted these researches, as to our ignorance respecting some of the fundamental problems of general physiology,—the solution of which would alone afford the necessary data for determining the most important questions relating to the action of poisons.

One of the fundamental points connected with this subject, and one which has attracted the greatest attention, is, as to the manner in which the more rapidly fatal poisons produce death: whether they must necessarily be absorbed and carried into the blood, before they can give rise to any general effects; or these effects may be the result of an action they exert on the nerves of the part to which they are directly applied, and which may therefore occur independently of their being absorbed? It is on this point that physiologists have differed; and most of the experiments that have been performed on the subject, during the last twenty-five years, have been instituted principally with a view of determining this question. Yet simple as the nature of the problem might appear, and notwithstanding all the attention that has been given to it, as yet, no decisive evidence has been brought to bear on the subject, or such, as in the opinion of most physiologists, is capable of definitely deciding the question. Some experiments which were performed a few years since, and were published in the *Ed. Med. and Surg. Journ.*, would I had hoped have been sufficiently conclusive to have decided the controversy. But as the conclusions which these experiments led me to have been called into question by Dr. Christison, in the last edition of his work on poisons, and also by Mr. Taylor, I propose to take a short review of the facts which have been published in my two former memoirs on this subject, and also to relate some recent experiments that have been performed, in the hope that the observations I have now to bring forward will be considered sufficiently conclusive to decide this long disputed question.

As to the great importance of our arriving at some definite and just conclusion on this point, there can be no doubt, when we consider how important, in the hands of the physiologist, is the class of substances whose action we are investigating. They are to him, in fact, what to the chemist are his reagents: the substances by means of which he introduces certain modifications in the living organism, in a manner analogous to that in which the chemist modifies the composition and properties of unorganized compounds by the various reagents he employs. It would be well, whilst employing the term poison, to remember its close analogy with that of reagent; the only difference being, that the latter term is applied more particularly to those compounds which are most used to determine changes or reactions in dead matter; whilst the term poison, applies to those bodies which we employ to determine reactions in living beings. An investigation, therefore, of the action of poisons, involves one of the most interesting subjects of research to the scientific physiologist; nor should these researches be confined to animals alone: the great service that has been rendered to morphological physiology, by a comparative study of form in the whole series of living beings, will be afforded likewise to physiological chemistry, by as extended a series of observations, performed with our physiological reagents or poisons.

The answer to the question, as to the manner in which poisons act, might, at first sight, be supposed to involve the whole of the phenomena connected with the changes they produce in living bodies; but such is not the meaning generally attached to it; and we could not be furnished with a more striking proof of the rudimentary state of physiology, than is afforded by the restricted sense in which this question is used. Far from being able to enter into the investigation of the molecular reactions on which the effects of poisons depend, we are obliged to confine ourselves to the determination of the most simple and most mechanical problems connected with their action; and although volumes have been published on the subject, and whole hecatombs of animals have been sacrificed, yet physiologists are yet undecided as to whether a poison must necessarily be absorbed before it produces any general effects. This question is evidently one of the most simple, and at the same time the most fundamental, of any connected with the action of poisons: it does not involve a knowledge of the chemical properties of the solids or fluids of the body; it does not even demand that we should be acquainted with the chemical composition of the poison we employ; we have not even to analyze the tissues on which we suspect the poison acts, for even its detection in these tissues would not throw any light on the subject. The research appears, indeed, to be one surrounded with but little difficulty, and yet, how much labour has been spent on it, without arriving at any satisfactory result.

It will be well, before proceeding farther, to endeavour to trace out the causes that have led to this want of success on apparently so simple a subject. There are, undoubtedly, many who will attribute it to the uncertainty which they suppose to be necessarily inherent to all experimental researches on animals; and who will thus endeavour to support that opinion which would deprive us, in elucidating the most complicated phenomena of matter, of that powerful lever of research, which has been so successfully used in almost every other branch of science. It may be well, indeed, for the speculator on physiological phenomena, to repudiate a method of research which involves a great deal of disagreeable labour, and the sacrifice of much time, but it must eventually be discovered that the most important advances in physiology will be attained by means of experimental investigation. If the experimental researches on the action of poisons have not led to any definite results, it is not owing to any fault inherent to the method itself, but on account of this method not having been followed out, in accordance with those rules by which every scientific inquiry should be conducted.

In order to arrive at any satisfactory result in an experimental investigation on the absorption or non-absorption of poisons, there was but one physiological fact which required to be known previously to entering on such an investigation, as it involves data which are indispensable in determining the question; this was, the time required for a poison to be conveyed by the blood from one part of the system to another; yet, all the earlier experiments on the action of poisons, were undertaken without any correct data on this point, and, in fact, under the influence of most erroneous ideas on the subject; and it is not until within the last few years that the experiments of Hering and myself, have afforded more correct data on the time occupied by the blood in circulating through the system.

It seems really surprising, that the manifest contradictions furnished by these experiments on poisons, did not lead to the suspicion that the data on which their action was explained must be wrong. For, on the one hand, it was found that poisons would give rise to symptoms of their action, and in fact destroy life, in a much shorter time than was believed necessary for them to be absorbed and carried by the blood over the system; *ergo*, they must act by impressions conveyed through the nerves. But, on the other hand, it was ascertained that a poison applied to a large surface, abundantly supplied with nerves, did not produce any general effects as long as it was prevented from mixing with the blood; *ergo*, they would not act by impressions conveyed through the nerves. Such an evident contradiction in the conclusions derived from these experiments, instead of leading to any doubt as to the correctness of the data on which they were founded, merely served to give rise to a new theory, which endeavoured to conciliate these opposing facts by introducing fresh errors into the investigation. I allude to the theory of Messrs. Addison and Morgan, which served to propitiate the believers in absorption, by finding that it was necessary that a poison should enter the blood-vessels before it could act, but that, when there, its farther effects were in accordance with the rules of sympathy, or owing to an impression conveyed through the nerves distributed on the inside of these vessels. This bastard theory on the action of poisons was that which, at the time I commenced my investigations on this subject, was most generally admitted; but as it was soon proved that every fact brought forward in support of it was erroneous, opinion at present seems to be again falling back on the old explanation, viz., that some poisons act by an impression they produce on the nerves of the part to which they are directly applied, whilst others produce their effects only when absorbed.

The experiments I have performed on this subject, have furnished me with a mass of evidence which, without a single exception, leads to the conclusion that the absorption of a poison must take place before it can give rise to any general effects. After having ascertained the correctness of the views of Hering in regard to the circulation, and having extended these researches, so as to ascertain the time required for the blood to circulate from one part of the system to another, in different species of animals, I was furnished with the necessary data for entering on the investigation of the action of poisons.

My researches on the circulation had proved, that the time required for the blood to pass from the jugular vein, and to be circulated through the body was, in the horse sixteen seconds, in the dog twelve seconds, in the fowl six seconds, and in the rabbit four seconds; and it now only remained to be seen if a poison, introduced into the veins, would give rise to any symptoms of its action, in a shorter time than these facts showed was required for it to be circulated through the system. Should such be the case, then, it was evident that the effects of the poison *must be* the result of an action on the nervous centres.

propagated through some other channel than that of the circulation. If, on the other hand, it was found, that between the time of the introduction of the poison into the veins, and the appearance of the first symptoms of its action, a sufficient interval always elapsed for it to be diffused over the system through the medium of the blood, which interval would vary in different animals according to the greater or less rapidity of the circulation, we then have conclusive evidence that it is by being absorbed and conveyed to the nervous centres that these poisons act.* A carefully conducted series of experiments, in which all the more rapidly fatal poisons were used, proved that in no instance did these substances show any symptoms of their action in a shorter space of time than that which would suffice for their general distribution through the system; it was found that when large doses of the most rapidly fatal poisons were introduced into the veins, they did not, in the horse, give rise to any symptoms of their action in less than sixteen seconds, in the dog, in less than twelve seconds, in the fowl, in less than six and a half seconds, and in the rabbit, in less than four and a half seconds.

These facts furnish us with a twofold proof as to the actions of poisons. In the first place, they show the improbability of their acting through the medium of impressions made on the nerves, by showing that they require a much longer time to act in some animals than in others; whereas, we cannot suppose that a nervous impression is much longer in reaching the sensorium in a horse, than in a rabbit. They also show that at the moment that the action of the poison on the nervous centres first shows itself, it has already been conveyed to these organs by the blood, so that there is no occasion to invoke the doctrine of sympathy to explain its action. The deductions arrived at by these facts are much strengthened when it is shown by experiments, from which I endeavoured to exclude every source of fallacy, that poisons will not act when applied to a part, the connections of which with the central parts of the nervous system are unimpaired, provided they are prevented from entering the general circulation. For the details of these experiments, I must refer to the *Edin. Med. and Surg. Journ.*, vol. liii. p. 55.

I shall now proceed to offer some remarks on the criticism which both Dr. Christison and Mr. Taylor have made on my experiments, in the last edition of their treatises on poisons. In the first place, they state, that my aim in performing these experiments was to support a preconceived theory, rather than to elucidate the truth; secondly, that my observations are not entitled to so much confidence as are those of others who have preceded me; and, lastly, that the conclusions I have arrived at, are opposed to facts which they believe they have observed. I must, before proceeding any farther, apologize for the egotistical statements which these remarks will necessarily oblige me to make; but I do this with the less regret, as, by showing the falseness of the grounds on which these gentlemen endeavour to invalidate my testimony, I shall add additional weight to the facts I have brought forward.

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* The poisons more directly alluded to, are those which evidently destroy life by their action on the nervous system.

I certainly must repudiate the imputation that is attempted to be cast on my experiments, by saying that they were undertaken to support a particular theory, for I believe I entered on these investigations with a mind much less likely to be prejudiced by erroneous views than those who had preceded me. I certainly had endeavoured, before proceeding to the investigation of the action of poisons, to satisfy my mind as to the truth of the data, a knowledge of which was necessary for its successful elucidation; and if, in so doing, I had arrived at new truths, which led me to conclude that many of the previous observations on this subject might be erroneous, I know not how this additional knowledge could incapacitate me from conscientiously undertaking an investigation, in which these newly discovered facts should find their application. If, in support of the facts which I had brought forward to prove the rapidity of the circulation, it had been necessary to show that poisons could only act when absorbed into the blood, I certainly might have had my mind prejudiced in favour of such a theory; but the proofs of the rapidity of the circulation, in different species of animals, were arrived at by experiments which were perfectly independent of the question as to the action of poisons, and would not have been at all shaken had they been found to act by sympathy, or nervous impressions. If, early in my researches, I adopted the theory of the absorption of poisons, it was that this theory was found to harmonize with the facts that I had observed, and although some of these facts were opposed to the observations of others, yet, as these observations had evidently been made under the influence of erroneous impressions, I would not allow them to have that weight which the names of their authors might otherwise have demanded for them. It must be evident, I think, to every impartial observer, that Dr. Christison himself was far more likely to labour under preconceived views than myself, for placing, as he evidently does, the greatest reliance on the facts brought forward by Sir B. Brodie and others, as to the instantaneous action of poisons. I believe it to be impossible for so philosophical a mind as that of the author of the treatise on poisons, not to have been imbued with the idea that they *must act* by an impression conveyed through the nerves, as this is the *only logical* deduction which could be derived from such data, particularly when we remember the views that were then prevalent as to the time required for the circulation of the blood.

As to how far my observations are worthy of credit above those of others, this is a point which must eventually be decided by others besides Dr. Christison and Mr. Taylor; but I would make one remark on an observation of Dr. Christison's, concerning the accuracy of my statements in regard to the intervals of time at which the phenomena occurred. Dr. C. states, "It is not unreasonable to claim for Sir B. Brodie, Dr. Freer, Mr. Macaulay, and Mr. Taylor, all of them practitioners of experience, the faculty of noting time as accurately as Dr. Blake himself." Now, without wishing to deny to any of these gentlemen the faculty of noting small intervals of time, I would observe, that I consider myself to have possessed some advantages in this respect over those who had preceded me; for, before commencing my researches on the action of poisons, I had been occupied for some time in experiments in which it was essential that short intervals of time should be strictly noticed, and I had thus acquired some practice in observing physiological phenomena, under this point of view. At the commencement of my experiments on the action of substances introduced into the blood, I strongly experienced the difficulty that exists in accurately noting the periods at which physiological phenomena occur, particularly when they follow each other with rapidity. In fact, I have to regret that some of the experiments published in my first memoir on this subject contain errors, on account of my not having then acquired the habit of accurately noting time; but, independently of the advantages which my previous experiments had given me in noting time, they had also shown me the importance of paying attention to short intervals of time in observing physiological phenomena—a fact which had never been so fully recognized by any who had preceded me, and who, therefore, were not likely to take those precautions which I adopted, in order to arrive at correct data on this point. But it is not on my own observations alone that the facts I have stated rest. Dr. Sharpey, who assisted Dr. Christison in his experiments, was also present when many of my experiments with conia and hydrocyanic acid were performed, and could bear testimony as to the accuracy of the facts recorded.

As regards the objection raised against my observations, that they are all of a negative character, and therefore cannot invalidate the affirmative testimony of those "who had perfectly well observed what I had not been fortunate enough to witness," I would remark that this objection loses much of its force when we consider under what erroneous impressions these former observations had been made, and also that my conclusions do not depend on a single experiment, in which I might possibly not have witnessed what some more fortunate experimenter had found; but that such should be the case in a long series of experiments, varied in many ways, and more comprehensive than any of those which had been before performed, is a supposition too improbable to be entertained.

Before proceeding to criticize the *facts* which have been brought forward as opposed to the conclusions I have arrived at, I regret to have to notice a mis-statement, which both Dr. Christison and Mr. Taylor have made, as regards my views on the action of poisons, and by means of which they have endeavoured to prove that the results I have arrived at must be false. Both these gentlemen state, when discussing the subject of the general action of poisons, that I have arrived at the conclusion that no poison will act on an animal in less than nine seconds; and then, having brought forward instances in which hydrocyanic acid had even produced death in a shorter time than I had stated was required for it to give rise to the first symptoms of its action, they, without the slightest difficulty, prove that my conclusions must be erroneous. Now, in the memoirs before alluded to, I state that in *the dog* a period of nine seconds is required for a poison, that is *introduced into a vein,* to give rise to the first symptoms of its action. Nor can this statement be at all invalidated by Dr. Christison and Mr. Taylor, finding that *hydrocyanic acid,* when put *into the mouth* of a *rabbit,* will even kill the animal in less than nine seconds; for I have proved, and these gentlemen have copied the statement in other parts of their treatises, that, in the *rabbit,* the circulation is fully *three times as rapid* as in the dog, so that a poison may only require one third of the time to act in the former animal to what it requires in the dog; and I have also shown that a volatile poison like hydrocyanic acid will act more rapidly when applied to the tongue than when introduced directly into the veins, on account of its being inhaled into the lungs, and thus finding a shorter way to the brain, than when it has to pass through the right cavities of the heart. Had Dr. Christison and Mr. Taylor fairly stated these facts, their observations, that hydrocyanic acid would kill in less than nine seconds, would not have so cleverly overturned my conclusions. Had these gentlemen succeeded in proving that, in the rabbit, or in the cat, hydrocyanic acid, when applied to the mouth, will produce its effects in less than two seconds and a half, this fact would have been inconsistent with the views I had supported; but, notwithstanding their statements about the instantaneous action of this poison, I believe they have never seen it act in a shorter time than that above stated.

I shall now proceed to notice the facts brought forward by these gentlemen, which they consider as supporting the theory of the sympathetic action of poisons. It would appear that the only experiments they have performed on this subject since the publication of my papers, have been made with concentrated hydrocyanic acid, on cats and rabbits. It is unfortunate that, in endeavouring to test the correctness of a theory which is of considerable physiological importance, these gentlemen should not have better understood the nature of the problem to be solved; as then they would not have selected, for elucidating it, means which were precisely those least calculated to throw any light upon it, and in the use of which it was the most difficult to guard against sources of error.

In selecting cats and rabbits to perform their experiments on, they could not have chosen worse; for in these animals the rapidity of the circulation is such, that the difference in the interval which should elapse between the application of a poison and the appearance of the first symptoms of its action, would not, according to the one or the other theory, be more than two and a half or three seconds; and I shall presently show that the determination of even this small interval is rendered doubly difficult by employing hydrocyanic acid in these experiments. Had their experiments been performed on horses, or even on full grown dogs, the difference in the time in which a poison should act, according to the one or the other theory, would have been an interval much more easily observed. The extreme volatility of the concentrated hydrocyanic acid renders it but little fitted for performing experiments of this sort, particularly on the smaller animals, for it is necessary to use care that the acid should not be brought near the mouth of the animal until the moment that it is to be applied, otherwise the previous inhalation of the vapour would totally vitiate the experiment. Its volatility also enables it, when applied to the tongue, to find a shorter way to the brain than would be the case with a poison which could not be volatilized so as to pass directly into the lungs; and this tends to render the interval that should be observed on the supposition of its absorption still shorter, and more difficult to be noted.

Now, to the correct appreciation of this short interval of two and a half or three seconds, there appears to me to be an obstacle which renders it almost impossible for us to avail ourselves of these means for deciding which theory of the action of poisons is correct. This obstacle arises from the pain caused by the application of any quantity of the acid to the mucous membrane of the mouth. Owing to its extreme volatility, its sudden evaporation will cause great cold and pain, and I believe its vapour will, under these circumstances, produce irritation of the glottis;—from both these causes, struggles instantly follow the application of the poison, and it is almost impossible to distinguish these struggles from the first symptoms of its action on the nervous centres, which so rapidly follow. I have no doubt but these considerations will afford an explanation of the cases of instantaneous action, which both Dr. Christison and Mr. Taylor state that they have observed.

The whole of the recent experiments with this substance, published by Dr. Christison, with the exception of one, tend to prove that the acid acts by absorption; as they show that a sufficient interval elapsed, between the application of the poison and the appearance of the first symptoms of its action, for it to have reached the nervous centres. The only exceptional experiment was one in which the acid was used in sufficient quantity to produce pain and struggles at the moment of its application, and I have no doubt but that these struggles were regarded as the results of its poisonous action. On the previous experiments, performed by Dr. Christison, with conia, I must still be permitted to doubt; as, in those which I made with this poison, I never observed it produce instantaneous effects. In these experiments also, Dr. Christison appears to have chosen those re-agents which were best fitted for leading him into error; for they were performed on young animals, in which the rapidity of the circulation is so much greater than in those which are full grown.

The evidence which Mr. Taylor brings forward in support of the sympathetic action of poisons, by quoting the statement of Addison and Morgan, that the Wourali poison would act even when it was not allowed to reach the brain, does not require any comment. But when the sources of fallacy which vitiated these experiments with the Wourali poison had been pointed out, he should not have brought them forward in a scientific treatise on poisons without, at least, stating the objections to which they were open.

I have performed some additional experiments on the action of these poisons since the publication of my former researches; but as they are perfectly analogous to the facts that are already before the public, I think it better not to occupy your pages by entering into details. It will, however, perhaps be useful to relate one of them, in order to show the precautions that were taken to avoid error. The experiment was performed on a rabbit, concentrated hydrocyanic acid being used as the poison. One end of a small glass tube was blown out before the blowpipe, so as to contain about half a drachm; this was filled with the poison, and the orifice of the tube closed with a glass stopper. The enlarged part of the tube containing the acid was introduced into the mouth of the rabbit, and placed between the points of a strong pair of forceps, so that by closing the forceps, at a given signal, the tube would be crushed and the acid escape into the mouth. The advantages of this arrangement were, that it insured the application of the acid at the instant being noted with much greater certainty than could be obtained by simply pouring it on the tongue, and I also avoided all danger of the animal previously inhaling the vapour of the poison, as the tube was five inches long, and well closed. On the poison being applied the animal was left at liberty, so that we could more readily observe when it lost the power of voluntary motion. At the moment of the application of the poison, the animal seemed to suffer considerable pain; it jumped off the table, and when on *the floor of the room, it was perfectly able to stand on its feet.* At two seconds and a half after the application of the poison it fell on its side, and it was dead in five seconds. This is but one of many experiments which have been performed on cats and rabbits, and in no instance have I observed instantaneous death, or even the instantaneous action of the poison.

Were the theory of the sympathetic action of poisons to be judged but by these facts alone, it would not be difficult to disprove the statement of Dr. Christison, that "the balance of testimony is in favour of those whose accuracy I impugn." But when we consider that this is but the weakest part of the testimony that can be brought forward, to prove that poisons can only act by absorption, when we take into service the facts furnished by so many experiments, which prove that the nerves are *incapable* of propagating the action of a poison from the part to which it is applied, and that it will not act unless it is allowed to enter the general circulation, we must admit that the theory of the sympathetic action of poisons, must either be supported by new and more conclusive evidence, or abandoned altogether. For these new facts I have as conscientiously sought as Dr. Christison and others; and if I have not been so fortunate as to discover them, it is that I believe they do not exist; and I think that, by using proper precautions to guard against error, they will escape the observation of others as well as myself.

St. Louis, *May* 3, 1849.